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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/866,279	05/30/1997	SUSAN M. DYMECKI	234805	9567

7590 02/11/2002

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EXAMINER	
BAKER, ANNE MARIE	
ART UNIT	PAPER NUMBER
1632	30

DATE MAILED: 02/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Application No.	Applicant(s)
08/866,279	Dymecki
Examiner	Art Unit
Anne-Marie Baker, Ph.D.	1632

Advisory Action

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED *Jan. 18, 2002* FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

a) ☒ The period for reply expires *6* months from the mailing date of the final rejection.

b) ☐ In view of the early submission of the proposed reply (within two months as set forth in MPEP § 706.07 (f)), the period for reply expires on the mailing date of this Advisory Action, OR continues to run from the mailing date of the final rejection, whichever is later. In no event, however, will the statutory period for the reply expire later than SIX MONTHS from the mailing date of the final rejection.

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *Jan 18, 2002*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will be entered upon the timely submission of a Notice of Appeal and Appeal Brief with requisite fees.

3. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search. (See NOTE below);

   (b) ☐ they raise the issue of new matter. (See NOTE below);

   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

   NOTE: *See Part A on attached sheet.*

4. ☐ Applicant's reply has overcome the following rejection(s):

5. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claim(s).

6. ☒ The a) ☒ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Part B on attached sheet.

7. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

8. ☒ For purposes of Appeal, the status of the claim(s) is as follows (see attached written explanation, if any):

   Claim(s) allowed: *NONE*

   Claim(s) objected to: *NONE*

   Claim(s) rejected: *1-49*

9. ☐ The proposed drawing correction filed on _____ a) ☐ has b) ☐ has not been approved by the Examiner.

10. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.

11. ☐ Other:

Anne-Marie Baker
ANNE-MARIE BAKER
PATENT EXAMINER

Advisory Action

Part A.

The proposed amendments (newly added Claims 50 and 51) would require new grounds of rejection under 35 U.S.C. 112, first and second paragraphs.

New rejections would be required under 35 U.S.C. 112, first paragraph, because the specification fails to teach how to use the claimed transgenic mice. As discussed in the Office Action of Paper No. 22 (mailed 10/25/00), the phenotype of a transgenic animal is unpredictable. In the absence of disclosure of a transgene-dependent phenotypic alteration, one skilled in the art would not know how to use the claimed transgenic mice. As discussed at pages 3-4 of the Office Action of Paper No. 22, the specification does not offer adequate guidance for making and using a mouse of the type claimed, wherein a transgene-dependent phenotypic alteration is produced. Thus, one skilled in the art would have been required to engage in undue experimentation in order to make and use the claimed transgenic mice.

New rejections would be required under 35 U.S.C. 112, second paragraph. Both Claims 50 and 51 recite proteins as members of the Markush groups, rather than genes or genes encoding the proteins recited in the Markush groups. With regard to Claim 51, the phrase "said developmental genes" lacks proper antecedent basis in Claim 15, which recites "genes controlling ... development of an organism." Furthermore, it is unclear whether Claim 51 is intended to be limited to "developmental genes" because Claim 15 is not limited to developmental genes, and so Claim 51 still encompasses all the other genes recited in the Markush group of Claim 15, with only the further limitation that the "developmental genes" (or rather, the genes controlling development of an organism) are now limited to the specific ones recited in the Markush group of Claim 51. Further, with regard to Claim 51, the metes and bounds of the terms "metabolic enzymes" and "growth/differentiation factors and their receptors" are indefinite. The Examiner does not find a definition for these terms in the specification that would define the metes and bounds.

Part B.

The Examiner accepts Applicant's declaration which demonstrates that the FLP recombinase version used in the Neuron paper was the F70L version and that the transgenes, both the FLP recombinase transgene and the indicator transgene were integrated into the genome by random integration. Thus, the Examiner acknowledges that the methodology used in the Neuron paper is the same methodology taught in the instant specification and that the use of the Hmgcr promoter to drive expression of the reporter gene is as contemplated in the instant specification. However, the present claims do not recite the complete phenotype of the transgenic mice claimed. Given that the specification only teaches how to use mice having certain phenotypes (*i.e.*, expression of a reporter gene in cells that have undergone FLP recombinase-mediated site-specific recombination), the claims must be limited to mice that actually exhibit those phenotypes. The specification is not enabling for mice that do not exhibit the disclosed transgene-dependent phenotype. See the Office Action of Paper No. 22 (mailed 10/25/00).

The claims must be congruent with the asserted utility of the invention, which in the instant case is cell fate mapping. The instant claims are not congruent with the asserted utility of cell fate mapping. For example, Claim 1 allows for the use of any promoter to drive expression of the FLP recombinase transgene. The specification only teaches how to use mice that have an FLP recombinase transgene under the control of a tissue-specific promoter **and** a reporter gene under the control of a non-tissue-specific (ubiquitous) promoter, wherein the reporter gene comprises a disruption comprising two Flp-recognition sequences in direct repeat orientation, such that the reporter gene produces active product only when in the recombined form.

Thus, the claims still encompass transgenic mice that the specification does not teach how to use.

Furthermore, numerous claims still cover gene **inactivation**, but the specification only teaches how to achieve partial inactivation. However, the specification does not teach how to use mice that only exhibit partial gene inactivation. For example, Claims 11, 24, and 36 encompass gene inactivation. See page 3, paragraph 4 of the Office Action of Paper No. 26 (mailed 7/18/01) which states that only partial gene inactivation can be accomplished and the specification does not demonstrate a phenotype produced by a deletion resulting in a null mutation because partial gene inactivation is not really a null mutation if only some cells have the deletion. This argument has not been addressed. Applicants apparently

attempted to address this issue at page 7, paragraph 2, but instead started arguing for a use for partial gene **activation**, rather than **inactivation**.

Thus, the claims still encompass transgenic mice that the specification does not teach how to use.

The rejection of claims 1-49 under 35 U.S.C. 112, first paragraph, is maintained for reasons of record.